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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/942,596	08/31/2001	Nobuko Yamamoto	35.C15718	7458

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EXAMINER

FREDMAN, JEFFREY NORMAN

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 03/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/942,596	Applicant(s) YAMAMOTO ET AL.	
	Examiner Jeffrey Fredman	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 January 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 and 9 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 13, 2005 has been entered.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-6 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Chee et al (Science (1996) 274:610-614)

Chee teaches a method of claims 1, 2 and 9 for identifying an unknown base sequence present in a target single stranded nucleic acid (see abstract) comprising the steps:

(a) preparing a probe array in which single stranded nucleic acid probes are arranged as isolated spots on a substrate, the probes each having a base sequence complementary to one of plural base sequences expected to be the unknown base sequence (see page 610, column 2 to page 611, column 1),

(b) reacting a single stranded nucleic acid, which has a base sequence fully complementary to a base sequence of one of the single stranded nucleic acid probes and is fluorescence labeled with the probe array under conditions that single stranded nucleic acids complementary to each other form a double stranded nucleic acid (see figure 1, panel C, top array and page 613, note 12)

removing the unreacted labeled single stranded nucleic acid (see page 613, note 12 and note 13),

measuring fluorescence intensity of each spot of the probe array to obtain a first template pattern showing a relationship between location of the probes and fluorescence characteristics (see page 614, notes 15, 17 and 21)

(c) performing the same operation as the step (b) for each of the remaining single stranded nucleic acid probes and obtaining template patterns of each probe showing a relationship between location and fluorescent characteristics of the probes (see figure 1, panel C, top array, and pages 613 and 614),

(d) performing the same operation as step (b) using a sample containing the target single-stranded nucleic acid of unknown base sequence to obtain a sample pattern showing relationship between a position and fluorescent characteristic (see figure 1, panel C, bottom array and pages 613 and 614)

(e) comparing the sample pattern obtained in step (d) with n pieces of template patterns obtained in steps (b) and (c), to identify a template pattern showing substantially the same pattern as the sample pattern and identifying the base sequence of the single stranded nucleic acid used from the preparation of the identified template

pattern as the unknown base sequence of the target single stranded nucleic acid (see page 611, figure 1 and column 1 and page 612, figure 2 and columns 1-3, where Chee expressly notes "The array was used to successfully detect three disease causing mutations in a mtDNA sample from a patient with Leber's hereditary optical neuropathy. In addition, we detected a total of seven errors and new polymorphisms from previously unsequenced regions (see page 612, column 3).")

(f) identifying the base sequence of the single stranded nucleic acid used for the preparation of the identified image template pattern as the base sequence of the target (see figure 3, for example, where the pattern is used to identify a mismatch, thereby determining a base sequence in a target nucleic acid),

Chee further analyzed the probe arrays to calculate a mean value of fluorescent intensities (see page 614, note 18) and then a difference was calculated between the fluorescence intensity of a reference array without a mismatch and the mean value of fluorescent intensities of the double stranded nucleic acids having a one or greater base mismatch (see page 614, note 16 and page 611, column 3) and

(g) Chee expressly notes regarding comparison of one and two mismatches to a control that "The marked decrease in target hybridization intensity, over a span of 20 nucleotides, is shown for a single base polymorphism as position 16,223 (Fig. 2A). The footprint is enlarged when two polymorphisms occur in close proximity (within 20 nucleotides) (Fig. 2B).(see pge 611, column 2)". Chee analyzes each of the positions to show a relationship between location and the fluorescent characteristics of the probes (see page 614, note 16 and page 611, column 3 and figure 2).

(h) Chee compares the sample pattern obtained from the unknown with the known sample pattern to identify the base sequence (see page 612, column 3 and page 614, notes 16 and 18).

With regard to claim 3, Chee determines a two valued pattern using two colors (see figure 2) and has a threshold intensity value (see page 614, note 18, where at least 50 counts above background is required).

With regard to claims, 4 and 5, Chee teaches probes in the range from 15 nucleotide oligomers (see page 610, column 3).

With regard to claim 6, Chee teaches single base pair mismatch detection (see figure 1).

Response to Arguments

4. Applicant's arguments filed January 13, 2005 have been fully considered but they are not persuasive.

Applicant argues that the current method is distinguished from Chee because it uses as emphasized repeatedly by Applicant, "plural" template patterns. However, this argument is not persuasive for a variety of reasons. For claims 1-6, the first and often central problem is that the claims include no requirement for "plural" template patterns. Claim 1 requires no more than two template patterns, a first pattern and a second pattern. Only claim 9 uses the term plural.

When addressing the word "plural" in claim 9, the phrase "a plurality of sites in a region" clearly refers to a more than one nucleic acid mutation in a target nucleic acid. However, it is absolutely clear from Chee that Chee is analyzing the position of multiple

sites. For example, figure 3, panel C shows image patterns at several different sites in the target, the mitochondrial genome. This meets the "plurality of sites in a region" limitation.

Chee is clearly analyzing the results by measuring the fluorescent intensity. The absence of a signal relative to the presence of a signal is the strongest type of comparison possible, and it is shown by Chee throughout his paper.

When Applicant argues that Chee does not disclose obtaining a template pattern for each probe spot, Applicant is reading something into the claim that is not there because it is clear that Chee is obtaining a pattern at each position. Chee is also certainly comparing the result to other template patterns, since a pattern which shows no mismatch differs from the pattern showing a match. Further, figure 2 is an express comparison of different patterns. With regard to the question of whether Chee can detect two closely related mutations, this element is not in the claims in any way and is entirely irrelevant. However as a factual matter, Applicant is incorrect in citing pages 611 and figure 2 legend to argue that closely related mutations would not be detected by the method of Chee. These portions of the Chee reference make no such comment and the skilled practitioner would expect the Chee method to function on mutations that were closely related because the tiled array would give different signals from two closely related mutations than from a single mutation or from wildtype at the same position.

Therefore, Applicants arguments are not found persuasive and the rejection over Chee is maintained. Chee remains anticipatory with regard to the claims.

Conclusion

5. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1637

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Jeffrey Fredman
Primary Examiner
Art Unit 1637

3/4/05